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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,229	04/23/2001	Venkata-Rangarao Kanikanti	LEA 33 253	8002

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EXAMINER
SHEIKH, HUMERA N

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 12/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/787,229	Applicant(s) KANIKANTI ET AL.	
	Examiner Humera N. Sheikh	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2002 (paper no.9)* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Acknowledgement is made of the receipt of the request for Extension of Time (2 months) and the Amendment, both filed 10/10/02.

The amendment (filed 10/10/02) for claims 1-8 and 12 has been entered.

The 35 U.S.C. 112 second paragraph rejection has been *withdrawn* by virtue of the amendment.

The applicant's arguments regarding the 35 U.S.C. 102 (b) rejections were found to be persuasive since the prior art does not anticipate the instant invention. As such, the 35 U.S.C. 102 (b) rejections have been *withdrawn.*

Claims 1-8 and 12 are pending. Claims 1-8 and 12 remain rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-8 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jenkins *et al.* (EP 0 205 282 B1) or Jenkins *et al.* (US Pat. No. 4,940,587).

Jenkins et al. (EP 0 205 282 B1 and US Pat. No. 4,940,587) teach a process for the preparation of a sustained release, oral pharmaceutical composition, comprising a hydrophilic polymer HPC (hydroxypropyl cellulose), (average molecular weight of greater than 200,000 and greater than 500,000), and a pharmaceutically active compound, wherein the percentages of HPC appear to fall within the claimed amounts and the active-compound polymer mixture is formed into coated granules having a particle size of less than 1000 micrometers for use in oral administration dosage forms (see EP reference pages 2-4 and examples and US reference columns 2-3 and examples).

Jenkins et al. do not explicitly disclose a molar degree of substitution of at least three. This was discussed above. It is unclear whether Jenkins et al. teaches the different degrees of molar substitution being well above three. Assuming that these are

different and in the absence of showing otherwise, it is deemed obvious to one of ordinary skill in the pharmaceutical art to obtain a suitable degree of molar substitution through routine or manipulative experimentation to obtain the best possible results. The expected result would be a process for the preparation of a sustained release oral formulation having the same intended purpose and outcome using an effective degree of molar substitution as similarly desired by the Applicant.

Jenkins while teaching a process for the preparation of a sustained release, oral pharmaceutical composition, comprising a hydrophilic polymer HPC - hydroxypropyl cellulose having an average molecular weight of greater than 200,000 and greater than 500,000, with a concentration of the cellulose being preferably between 2% and 15% (page 3, lines 7-8), does not teach the applicant's claimed range of 40-95%. One of ordinary skill familiar in the pharmaceutical art could, through the use of routine or manipulative experimentation, obtain the best possible results. Furthermore, Jenkins clearly teaches the same ingredients for a similar intended purpose and therefore the expected results would also be the same.

Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made and there is ample motivation provided by the prior art to formulate an orally administrable pharmaceutical preparation comprising hydroxypropylcellulose in the specified concentration percentages because Jenkins explicitly teaches such a process wherein the hydroxypropylcellulose is found to exhibit particularly good qualities of adhesion and strength. The expected result would be a

method for the preparation of an improved sustained release oral pharmaceutical composition.

Response to Arguments

Applicant's arguments with respect to claims 1-8 and 12 regarding the 35 U.S.C. 102(b) rejections have been considered but are moot in view of the new ground(s) of rejection.

Applicant's arguments filed 10/10/02 have been fully considered but they are not persuasive. The applicant argued regarding the 35 U.S.C. 103(a) rejections for claims 1-8 and 12 by Jenkins (EP 0 205 282) or Jenkins (US Pat. No. 4,940,587).

Firstly, the applicant argued,

"Jenkins does not teach or suggest a pharmaceutical preparation containing 40-95% w/w hydroxypropylcellulose. Also, Jenkins does not teach or suggest formation of a mixture of 40-95% w/w hydroxypropylcellulose and a pharmaceutical into granules having 0.2-3.0 mm. Furthermore, Jenkins does not teach or suggest administration of said pharmaceutical preparation as a multiple-unit preparation.

Jenkins cites the term 'oral', but it is clear from the specification that the preparations according to Jenkins are not to be swallowed (col.1, para.3). On the contrary, the gist of Jenkins is to avoid swallowing of the preparation. The Jenkins preparations are to be applied buccally or nasally, that is remaining in the oral or nasal cavity, resulting in parenteral

administration. In contrast, the preparations according to the present invention are to be administered orally.

Finally, Jenkins does not teach or suggest the use of said preparation for a food-effect independent method for orally administering the pharmaceutical.

Since the cited references do not teach or suggest the elements of the claims, the claims are allowable under 35 U.S.C. 103(a)."

The applicant's remarks have been fully considered but are not found to be persuasive. The instant invention is drawn to a process for the production of an orally administrable multiple-unit sustained release pharmaceutical composition comprising the steps of: (a) combining hydroxypropylcellulose polymer (average molecular weight-250,000 to 1,200,000 and a molar degree of substitution of at least 3) in an amount from 40 to 95% by weight with a pharmaceutically acceptable compound to obtain a mixture of a compound; (b) converting said mixture into particles having a diameter of 0.2 to 3.0 mm; and (c) converting said particles into said orally administrable pharmaceutical composition.

Jenkins (EP '282 and US '587) teach a process for the preparation of a sustained release, oral pharmaceutical composition, comprising a hydrophilic polymer HPC - hydroxypropyl cellulose having an average molecular weight of greater than 200,000 and greater than 500,000, wherein the active-compound polymer mixture is formed into coated granules having a particle size of less than 1000 micrometers for use in oral administration dosage forms. Jenkins discloses that the concentration of the cellulose

is preferably between 2% and 15% (page 3, lines 7-8). The instant invention desires a concentration of 40-95%. Jenkins teaches the generic concept of including a hydrophilic polymer (HPC) having a high molecular weight in a sustained release oral formulation. Actually, the only difference observed between the prior art and the instant invention is that Jenkins teaches a lower concentration range of the hydroxypropylcellulose as compared with the applicant's claimed range of 40-95%. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. Furthermore, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

The applicant's remarks have been carefully considered, but are not found to be persuasive. The applicant argued in regards that the instant invention is an orally administered composition whereas Jenkins is buccally or nasally administered. This argument is not persuasive since Jenkins, in fact, explicitly teaches an *oral* pharmaceutical composition having sustained release (see claim 1). The composition is adapted to be applicable to the oral or nasal cavity. In addition, Jenkins teaches a similar end product as that of the applicant, in that the coated granules are compressed and converted to a solid dosage form (i.e., tablet) (claims 12-15). In essence, the oral, sustained release composition of Jenkins directly meets the applicant's claims of an oral pharmaceutical composition, regardless of the destined route of the dosage form, since

Jenkins clearly teaches an oral composition that must be administered through the mouth.

The applicant's arguments have been carefully considered, but are not found to be persuasive. The applicant argued, "Jenkins does not teach or suggest the use of said preparation for a food-effect independent method for orally administering the pharmaceutical."

This argument has been fully considered, but is not found to be persuasive and the examiner points out that Jenkins teaches an orally administrable pharmaceutical composition comprising the same ingredients, in similar amounts with a similar intended purpose as the applicant and therefore the properties of the solid dosage form would also be identical to the instant invention. Furthermore, it is of no moment that the prior art recognize each and every attribute of the instant invention, merely that the prior art recognize a similar dosage formulation processed in a synonymous manner, is sufficient. There is no significant difference between the prior art and the instant invention since Jenkins explicitly teaches a process for the preparation of a sustained release, oral pharmaceutical composition and the composition obtained thereof, comprising a solid unit dosage form of hydroxypropylcellulose in combination with active-compounds for oral dosage administration.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (703) 308-4429. The examiner can normally be reached on Monday through Friday from 7:00A.M. to 4:30P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

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